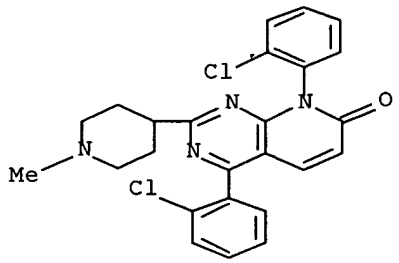
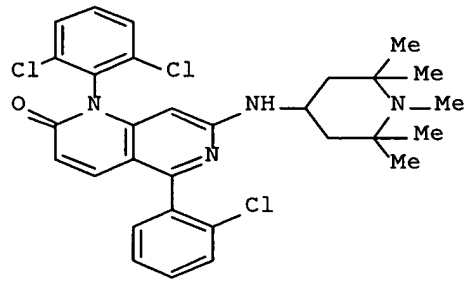
L7 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:384411 CAPLUS
DN 139:230713
TI A convenient synthesis of trisubstituted pyrido[2,3-d]pyrimidin-7-ones
AU Kasparec, Jiri; Adams, Jerry L.; Sisko, Joseph; Silva, Domingos J.
CS Medicinal Chemistry Department, GlaxoSmithKline, Collegeville, PA, 19426, USA
SO Tetrahedron Letters (2003), 44(24), 4567-4570
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier Science Ltd.
DT Journal
LA English
AB A novel, highly efficient and scalable route for the synthesis of trisubstituted pyrido[2,3-d]pyrimidin-7-ones was developed. The target compds. were synthesized in five steps from readily available reagents in about 40% overall yield.
IT **593277-87-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of trisubstituted pyrido[2,3-d]pyrimidin-7-ones via nucleophilic displacement followed by Suzuki coupling as the key steps)
RN 593277-87-3 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 4,8-bis(2-chlorophenyl)-2-(1-methyl-4-piperidinyl)- (9CI) (CA INDEX NAME)



RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/29/03

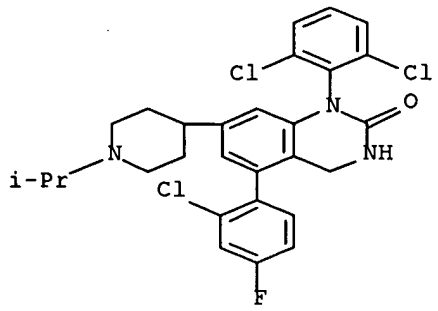
L7 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:91257 CAPLUS
DN 138:385389
TI p38 Inhibitors: piperidine- and 4-aminopiperidine-substituted naphthyridinones, quinolinones, and dihydroquinazolinones
AU Hunt, Julianne A.; Kallashi, Florida; Ruzek, Rowena D.; Sinclair, Peter J.; Ita, Ida; McCormick, Sherrie X.; Pivnichny, James V.; Hop, Cornelis E. C. A.; Kumar, Sanjeev; Wang, Zhen; O'Keefe, Stephen J.; O'Neill, Edward A.; Porter, Gene; Thompson, James E.; Woods, Andrea; Zaller, Dennis M.; Doherty, James B.
CS Department of Medicinal Chemistry, Merck & Co., Inc., Rahway, NJ, 07065, USA
SO Bioorganic & Medicinal Chemistry Letters (2003), 13(3), 467-470
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 138:385389
GI



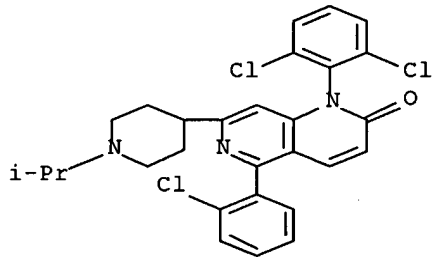
I

AB A series of C7-piperidine- and 4-aminopiperidine-substituted naphthyridinones, quinolinones, and dihydroquinazolinones were synthesized as highly potent inhibitors of both p38 mitogen-activated protein (MAP) kinase activity and tumor necrosis factor (TNF)-.alpha. release. The 4-aminopentamethylpiperidine naphthyridinone I, which was designed to block metab. at major 'hot spots', combined excellent inhibitory potency with good oral bioavailability in the rat.

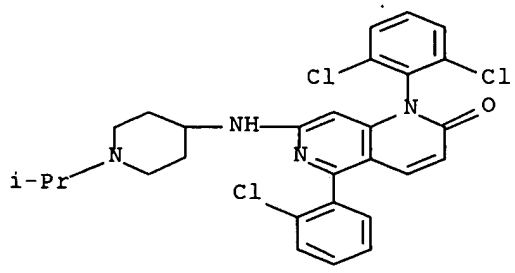
IT **444660-65-5**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(synthesis of piperidine and 4-aminopiperidine-substituted naphthyridinones, quinolinones, and dihydroquinazolinones as inhibitors of p38 MAP kinase and TNF-.alpha. release)
RN 444660-65-5 CAPLUS
CN 2(1H)-Quinazolinone, 5-(2-chloro-4-fluorophenyl)-1-(2,6-dichlorophenyl)-3,4-dihydro-7-[1-(1-methylethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)



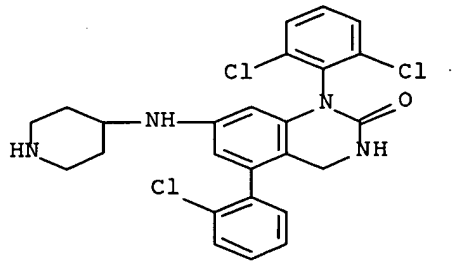
IT **444661-57-8P 444661-63-6P 444661-91-0P**
444661-92-1P 444665-12-7P 527680-12-2P
527680-13-3P 527680-15-5P 527680-16-6P
527680-17-7P 527680-18-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of piperidine and 4-aminopiperidine-substituted naphthyridinones, quinolinones, and dihydroquinazolinones as inhibitors
of p38 MAP kinase and TNF-.alpha. release)
RN 444661-57-8 CAPLUS
CN 1,6-Naphthyridin-2(1H)-one, 5-(2-chlorophenyl)-1-(2,6-dichlorophenyl)-7-[1-
(1-methylethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)



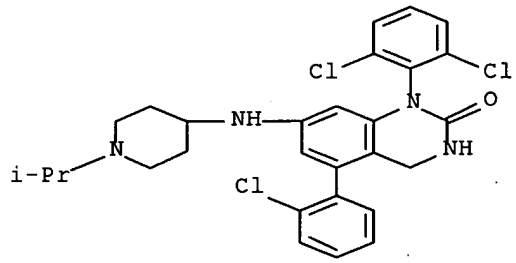
RN 444661-63-6 CAPLUS
CN 1,6-Naphthyridin-2(1H)-one, 5-(2-chlorophenyl)-1-(2,6-dichlorophenyl)-7-[[1-(1-methylethyl)-4-piperidinyl]amino]- (9CI) (CA INDEX NAME)



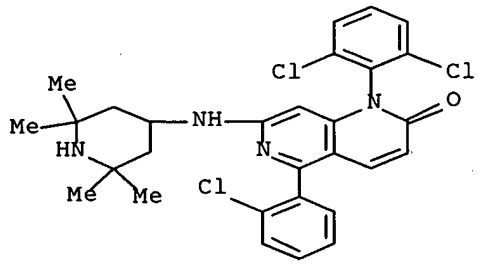
RN 444661-91-0 CAPLUS
CN 2(1H)-Quinazolinone, 5-(2-chlorophenyl)-1-(2,6-dichlorophenyl)-3,4-dihydro-
7-(4-piperidinylamino)- (9CI) (CA INDEX NAME)



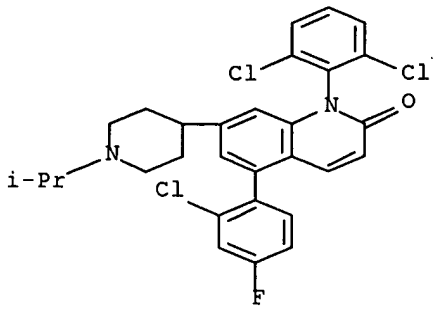
RN 444661-92-1 CAPLUS
CN 2(1H)-Quinazolinone, 5-(2-chlorophenyl)-1-(2,6-dichlorophenyl)-3,4-dihydro-
7-[[1-(1-methylethyl)-4-piperidinyl]amino]- (9CI) (CA INDEX NAME)



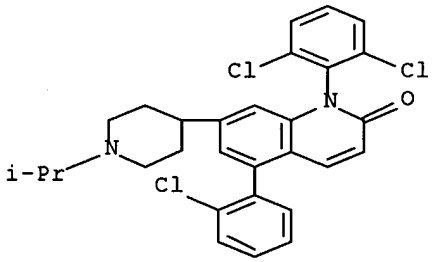
RN 444665-12-7 CAPLUS
CN 1,6-Naphthyridin-2(1H)-one, 5-(2-chlorophenyl)-1-(2,6-dichlorophenyl)-7-[(2,2,6,6-tetramethyl-4-piperidinyl)amino]- (9CI) (CA INDEX NAME)



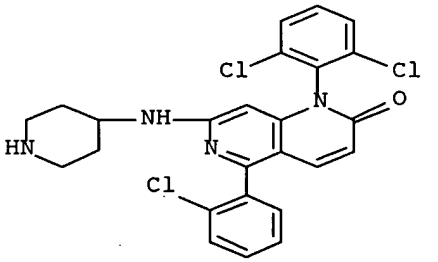
RN 527680-12-2 CAPLUS
CN 2(1H)-Quinolinone, 5-(2-chloro-4-fluorophenyl)-1-(2,6-dichlorophenyl)-7-[1-
(1-methylethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)



RN 527680-13-3 CAPLUS
CN 2(1H)-Quinolinone, 5-(2-chlorophenyl)-1-(2,6-dichlorophenyl)-7-[1-(1-methylethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

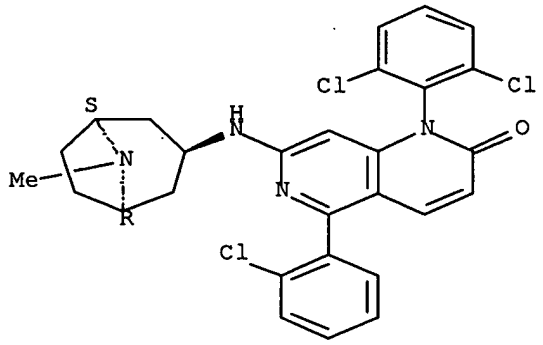


RN 527680-15-5 CAPLUS
CN 1,6-Naphthyridin-2(1H)-one, 5-(2-chlorophenyl)-1-(2,6-dichlorophenyl)-7-(4-piperidinylamino)- (9CI) (CA INDEX NAME)



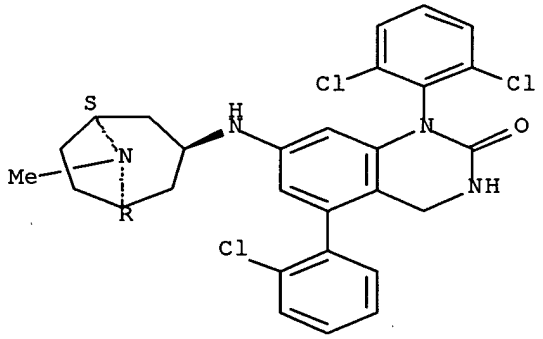
RN 527680-16-6 CAPLUS
CN 1,6-Naphthyridin-2(1H)-one, 5-(2-chlorophenyl)-1-(2,6-dichlorophenyl)-7-[[(3-endo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]amino]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

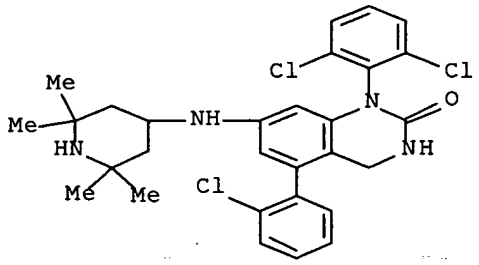


RN 527680-17-7 CAPLUS
CN 2(1H)-Quinazolinone, 5-(2-chlorophenyl)-1-(2,6-dichlorophenyl)-3,4-dihydro-
7-[[(3-endo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]amino]- (9CI) (CA INDEX
NAME)

Relative stereochemistry.

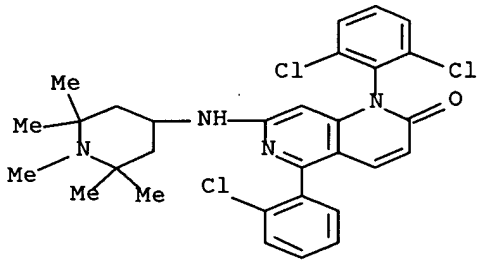


RN 527680-18-8 CAPLUS
CN 2(1H)-Quinazolinone, 5-(2-chlorophenyl)-1-(2,6-dichlorophenyl)-3,4-dihydro-
7-[(2,2,6,6-tetramethyl-4-piperidinyl)amino]- (9CI) (CA INDEX NAME)

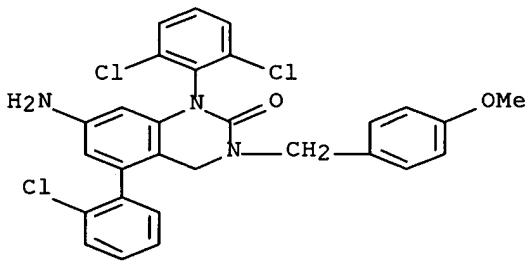


IT **527680-19-9P**
RL: PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological

study); PREP (Preparation)
(synthesis of piperidine and 4-aminopiperidine-substituted naphthyridinones, quinolinones, and dihydroquinazolinones as inhibitors
of p38 MAP kinase and TNF-.alpha. release)
RN 527680-19-9 CAPLUS
CN 1,6-Naphthyridin-2(1H)-one, 5-(2-chlorophenyl)-1-(2,6-dichlorophenyl)-7-[(1,2,2,6,6-pentamethyl-4-piperidinyl)amino]- (9CI) (CA INDEX NAME)



IT **444665-70-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(synthesis of piperidine and 4-aminopiperidine-substituted naphthyridinones, quinolinones, and dihydroquinazolinones as inhibitors
of p38 MAP kinase and TNF-.alpha. release)
RN 444665-70-7 CAPLUS
CN 2(1H)-Quinazolinone, 7-amino-5-(2-chlorophenyl)-1-(2,6-dichlorophenyl)-3,4-
dihydro-3-[(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2003:70672 CAPLUS

DN 139:143286

TI A novel P450-catalyzed transformation of the 2,2,6,6-tetramethyl piperidine moiety to a 2,2-dimethyl pyrrolidine in human liver microsomes: characterization by high resolution quadrupole-time-of-flight mass spectrometry and 1H-NMR

AU Yin, Wenji; Doss, George A.; Stearns, Ralph A.; Chaudhary, Ashok G.; Hop, Cornelis E.; Franklin, Ronald B.; Kumar, Sanjeev

CS Department of Drug Metabolism, Merck Research Laboratories, Rahway, NJ, USA

SO Drug Metabolism and Disposition (2003), 31(2), 215-223
CODEN: DMDSAI; ISSN: 0090-9556

PB American Society for Pharmacology and Experimental Therapeutics

DT Journal

LA English

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

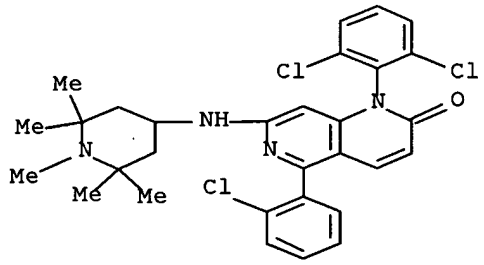
AB We describe herein a novel metabolic fate of the 2,2,6,6-tetramethyl-piperidine (2,2,6,6-TMPi) moiety to a ring-contracted 2,2-di-Me pyrrolidine (2,2-DMPy) in human liver microsomal incubations. The existence of this pathway was demonstrated for three compds. (I-III) of varied structures suggesting that this may be a general biotransformation reaction for the 2,2,6,6-TMPi moiety. The 2,2-DMPy metabolites formed in incubations of the three compds. with human liver microsomes were characterized by online high performance liq. chromatog. coupled to a high resoln. hybrid quadrupole-time-of-flight mass spectrometer. Suggested elemental compn. obtained from accurate mass measurements of the mol. ions and fragment ions of the metabolites clearly indicated the loss of a mass equiv. to C3H6 from the parent 2,2,6,6-TMPi functionality. Addnl. accurate tandem mass spectrometry data indicated that one of the original two gem-di-Me groups was intact in the metabolite structure. Proof of a ring-contracted 2,2-DMPy structure was obtained using 1H-NMR expts. on a metabolite purified from liver microsomal incubations, which showed only two geminal Me groups, instead of four in the parent compd. Two-dimensional correlation spectroscopy and decoupling expts. established aliph. protons arranged in a pyrrolidine ring pattern. The fact that the formation of 2,2-DMPy metabolites in human liver microsomes was NADPH-dependent suggested that this novel metabolic reaction was catalyzed by the cytochrome P 450 enzyme(s). Immunoinhibition studies in human liver microsomal incubations using anti-P 450 monoclonal antibodies and expts. with insect cell microsomes contg. individually expressed recombinant human P 450 isoenzymes indicated that multiple P 450 isoenzymes were capable of catalyzing this novel metabolic transformation.

IT **527680-19-9**

RL: PKT (Pharmacokinetics); BIOL (Biological study)
(novel P 450-catalyzed transformation of the 2,2,6,6-tetra-Me piperidine moiety to a 2,2-di-Me pyrrolidine in human liver microsomes)

RN 527680-19-9 CAPLUS

CN 1,6-Naphthyridin-2(1H)-one, 5-(2-chlorophenyl)-1-(2,6-dichlorophenyl)-7-[(1,2,2,6,6-pentamethyl-4-piperidinyl)amino]- (9CI) (CA INDEX NAME)

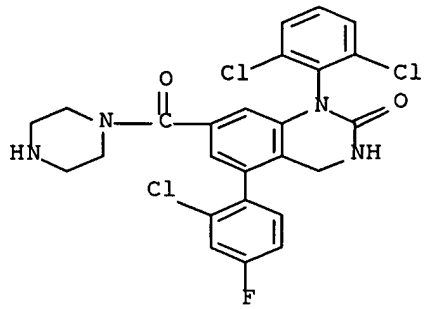


RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

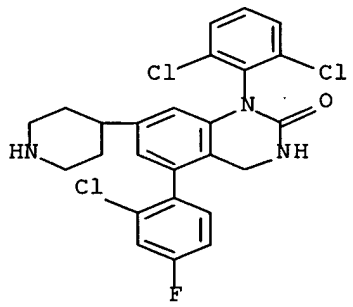
L7 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:943599 CAPLUS
DN 138:271641
TI Design and synthesis of potent, orally bioavailable dihydroquinazolinone inhibitors of p38 MAP kinase
AU Stelmach, John E.; Liu, Luping; Patel, Sangita B.; Pivnichny, James V.; Scapin, Giovanna; Singh, Suresh; Hop, Cornelis E. C. A.; Wang, Zhen; Strauss, John R.; Cameron, Patricia M.; Nichols, Elizabeth A.; O'Keefe, Stephen J.; O'Neill, Edward A.; Schmatz, Dennis M.; Schwartz, Cheryl D.; Thompson, Chris M.; Zaller, Dennis M.; Doherty, James B.
CS Department of Medicinal Chemistry, Merck Research Laboratories, Rahway, NJ, 07065, USA
SO Bioorganic & Medicinal Chemistry Letters (2003), 13(2), 277-280
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The development of potent, orally bioavailable (in rat) and selective dihydroquinazolinone inhibitors I (R = CO2Me, R1 = H, Br, 2-FC6H4, etc.; R = OMe, R1 = 2-Cl-4-FC6H3, 2,4-F2C6H3, 2-ClC6H4), II (R1 = 2-Cl-4-FC6H3, 2,4-F2C6H3, 2-ClC6H4, X = none, O, NH, CH2, CO, Y = CH, N) and III (R2 = Me, Et, CHMe2, etc.) of p38.alpha. MAP kinase is described. For example, III (R2 = CMe3) was prepd. via the Still coupling of I (R = OSO2CF3, R1 = 2-Cl-4-FC6H3) with 1-tert-butyl-4-(trimethylstannyl)-1,2,3,6-tetrahydropyridine. These analogs are hybrids of a pyridinylimidazole p38.alpha. inhibitor reported by Merck Research Labs. and VX-745. Optimization of the C-5 Ph and the C-7 piperidinyl substituents led to the identification of III (R2 = CMe3) which gave excellent suppression of TNF-.alpha. prodn. in LPS-stimulated whole blood (IC50=10 nM) and good oral exposure in rats (F=68%, AUCn PO=0.58 .mu.M h).
IT **444660-26-8**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of 1-(2,6-dichlorophenyl)quinazolinone derivs., their p38.alpha. MAP kinase inhibition, rat pharmokinetics, and inhibition of TNF-.alpha. prodn. in monocytes, THP-1 cells and human whole blood)
RN 444660-26-8 CAPLUS
CN Piperazine, 1-[[5-(2-chloro-4-fluorophenyl)-1-(2,6-dichlorophenyl)-1,2,3,4-tetrahydro-2-oxo-7-quinazolinyl]carbonyl]- (9CI) (CA INDEX NAME)

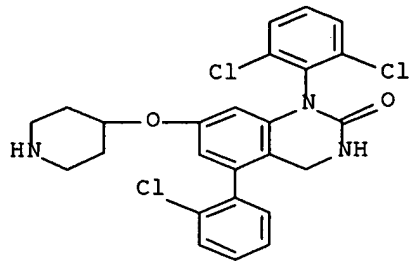


IT **444660-60-0P**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
PKT (Pharmacokinetics); RCT (Reactant); SPN (Synthetic preparation); BIOL
(Biological study); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 1-(2,6-dichlorophenyl)quinazolinone derivs., their p38.alpha. MAP kinase inhibition, rat pharmokinetics, and inhibition of
TNF-.alpha. prodn. in monocytes, THP-1 cells and human whole blood)
RN 444660-60-0 CAPLUS
CN 2(1H)-Quinazolinone, 5-(2-chloro-4-fluorophenyl)-1-(2,6-dichlorophenyl)-3,4-dihydro-7-(4-piperidinyl)- (9CI) (CA INDEX NAME)

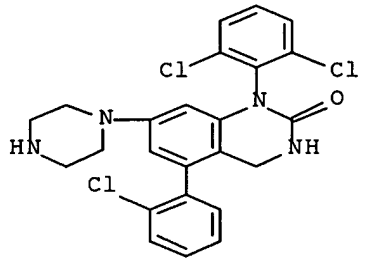


IT **444660-17-7P 444660-40-6P 444660-58-6P**
444660-59-7P 444660-62-2P 444660-63-3P
444660-64-4P 444660-65-5P 444660-66-6P
503184-90-5P 503184-92-7P 503184-93-8P
503184-94-9P 503184-95-0P 503184-96-1P
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of 1-(2,6-dichlorophenyl)quinazolinone derivs., their p38.alpha. MAP kinase inhibition, rat pharmokinetics, and inhibition of
TNF-.alpha. prodn. in monocytes, THP-1 cells and human whole blood)
RN 444660-17-7 CAPLUS
CN 2(1H)-Quinazolinone, 5-(2-chlorophenyl)-1-(2,6-dichlorophenyl)-3,4-dihydro-

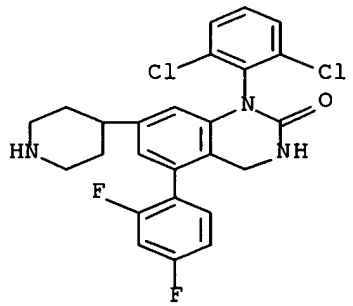
7-(4-piperidinyloxy)- (9CI) (CA INDEX NAME)



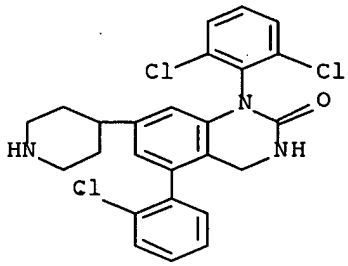
RN 444660-40-6 CAPLUS
CN 2(1H)-Quinazolinone, 5-(2-chlorophenyl)-1-(2,6-dichlorophenyl)-3,4-dihydro-
7-(1-piperazinyl)- (9CI) (CA INDEX NAME)



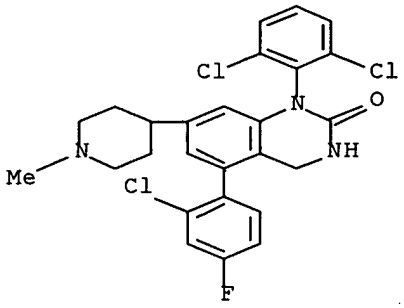
RN 444660-58-6 CAPLUS
CN 2(1H)-Quinazolinone, 1-(2,6-dichlorophenyl)-5-(2,4-difluorophenyl)-3,4-dihydro-7-(4-piperidinyl)- (9CI) (CA INDEX NAME)



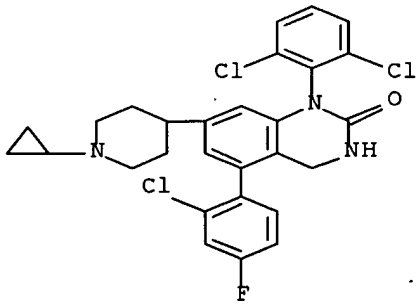
RN 444660-59-7 CAPLUS
CN 2(1H)-Quinazolinone, 5-(2-chlorophenyl)-1-(2,6-dichlorophenyl)-3,4-dihydro-
7-(4-piperidinyl)- (9CI) (CA INDEX NAME)



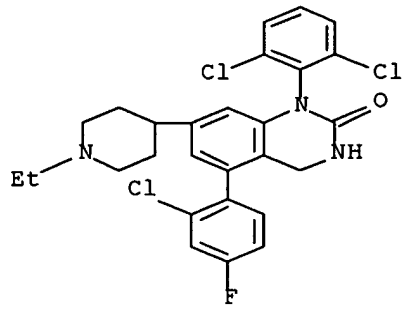
RN 444660-62-2 CAPLUS
CN 2(1H)-Quinazolinone, 5-(2-chloro-4-fluorophenyl)-1-(2,6-dichlorophenyl)-3,4-dihydro-7-(1-methyl-4-piperidinyl)- (9CI) (CA INDEX NAME)



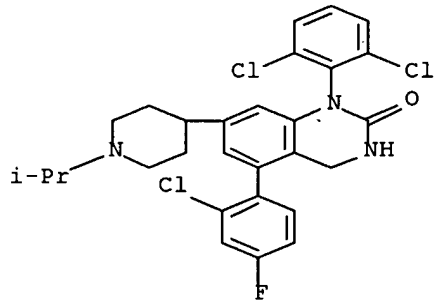
RN 444660-63-3 CAPLUS
CN 2(1H)-Quinazolinone, 5-(2-chloro-4-fluorophenyl)-7-(1-cyclopropyl-4-piperidinyl)-1-(2,6-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)



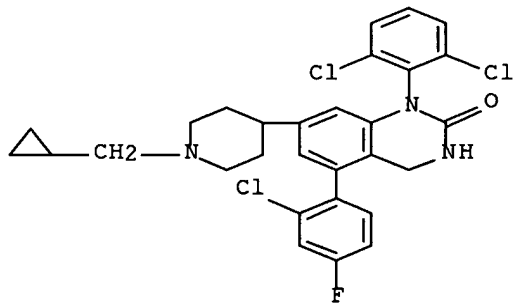
RN 444660-64-4 CAPLUS
CN 2(1H)-Quinazolinone, 5-(2-chloro-4-fluorophenyl)-1-(2,6-dichlorophenyl)-7-
(1-ethyl-4-piperidinyl)-3,4-dihydro- (9CI) (CA INDEX NAME)



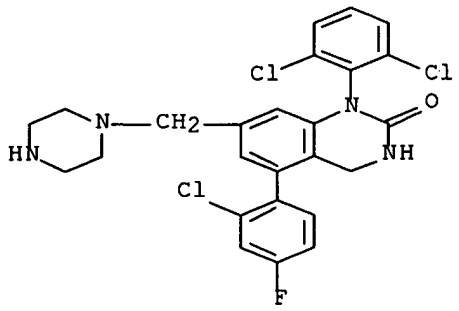
RN 444660-65-5 CAPLUS
CN 2(1H)-Quinazolinone, 5-(2-chloro-4-fluorophenyl)-1-(2,6-dichlorophenyl)-3,4-dihydro-7-[1-(1-methylethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)



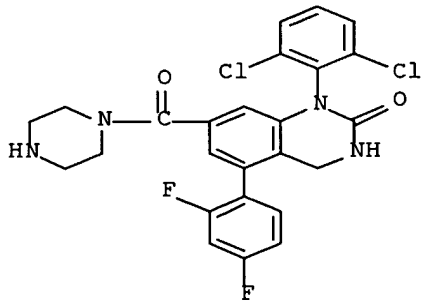
RN 444660-66-6 CAPLUS
CN 2(1H)-Quinazolinone, 5-(2-chloro-4-fluorophenyl)-7-[1-(cyclopropylmethyl)-4-piperidinyl]-1-(2,6-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)



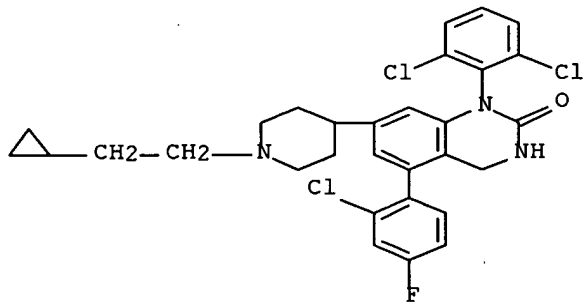
RN 503184-90-5 CAPLUS
CN 2(1H)-Quinazolinone, 5-(2-chloro-4-fluorophenyl)-1-(2,6-dichlorophenyl)-3,4-dihydro-7-(1-piperazinylmethyl)- (9CI) (CA INDEX NAME)



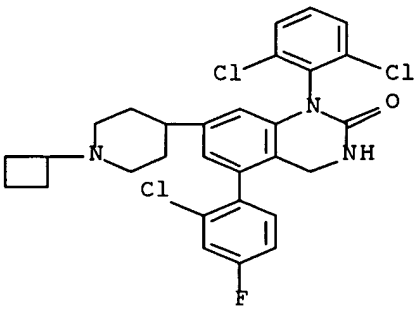
RN 503184-92-7 CAPLUS
CN Piperazine, 1-[[1-(2,6-dichlorophenyl)-5-(2,4-difluorophenyl)-1,2,3,4-tetrahydro-2-oxo-7-quinazolinyl]carbonyl]- (9CI) (CA INDEX NAME)



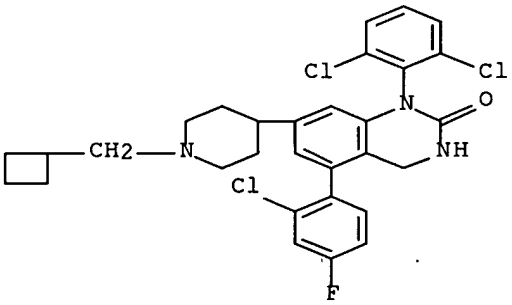
RN 503184-93-8 CAPLUS
CN 2(1H)-Quinazolinone, 5-(2-chloro-4-fluorophenyl)-7-[1-(2-cyclopropylethyl)-4-piperidinyl]-1-(2,6-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)



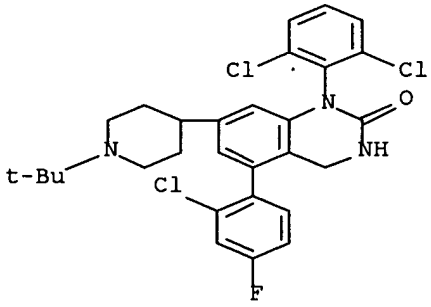
RN 503184-94-9 CAPLUS
CN 2(1H)-Quinazolinone, 5-(2-chloro-4-fluorophenyl)-7-(1-cyclobutyl-4-piperidinyl)-1-(2,6-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)



RN 503184-95-0 CAPLUS
CN 2(1H)-Quinazolinone, 5-(2-chloro-4-fluorophenyl)-7-[1-(cyclobutylmethyl)-4-piperidinyl]-1-(2,6-dichlorophenyl)-3,4-dihydro- (9CI) (CA INDEX NAME)

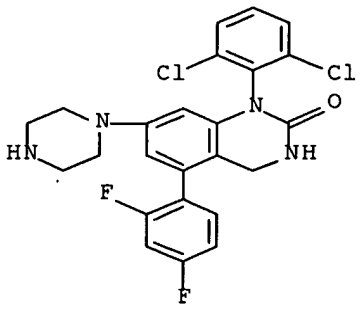


RN 503184-96-1 CAPLUS
CN 2(1H)-Quinazolinone, 5-(2-chloro-4-fluorophenyl)-1-(2,6-dichlorophenyl)-7-[1-(1,1-dimethylethyl)-4-piperidinyl]-3,4-dihydro- (9CI) (CA INDEX NAME)

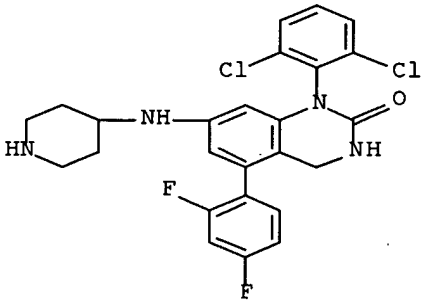


IT **444660-41-7P 444660-45-1P 444661-91-0P**
503184-88-1P 503184-89-2P 503184-91-6P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of 1-(2,6-dichlorophenyl)quinazolinone derivs., their p38.alpha. MAP kinase inhibition, rat pharmokinetics, and inhibition

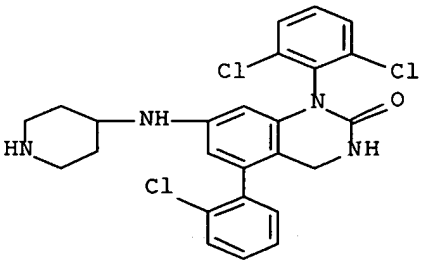
of
TNF-.alpha. prodn. in monocytes, THP-1 cells and human whole blood)
RN 444660-41-7 CAPLUS
CN 2(1H)-Quinazolinone, 1-(2,6-dichlorophenyl)-5-(2,4-difluorophenyl)-3,4-dihydro-7-(1-piperazinyl)- (9CI) (CA INDEX NAME)



RN 444660-45-1 CAPLUS
CN 2(1H)-Quinazolinone, 1-(2,6-dichlorophenyl)-5-(2,4-difluorophenyl)-3,4-dihydro-7-(4-piperidinylamino)- (9CI) (CA INDEX NAME)

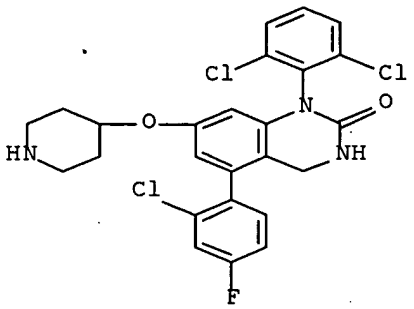


RN 444661-91-0 CAPLUS
CN 2(1H)-Quinazolinone, 5-(2-chlorophenyl)-1-(2,6-dichlorophenyl)-3,4-dihydro-
7-(4-piperidinylamino)- (9CI) (CA INDEX NAME)

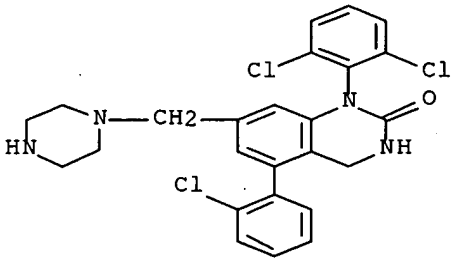


RN 503184-88-1 CAPLUS
CN 2(1H)-Quinazolinone, 5-(2-chloro-4-fluorophenyl)-1-(2,6-dichlorophenyl)-

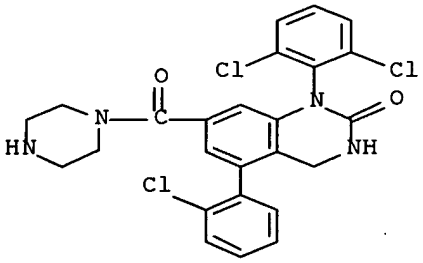
3,4-dihydro-7-(4-piperidinyloxy)- (9CI) (CA INDEX NAME)



RN 503184-89-2 CAPLUS
CN 2(1H)-Quinazolinone, 5-(2-chlorophenyl)-1-(2,6-dichlorophenyl)-3,4-dihydro-
7-(1-piperazinylmethyl)- (9CI) (CA INDEX NAME)



RN 503184-91-6 CAPLUS
CN Piperazine, 1-[[5-(2-chlorophenyl)-1-(2,6-dichlorophenyl)-1,2,3,4-tetrahydro-2-oxo-7-quinazolinyl]carbonyl]- (9CI) (CA INDEX NAME)



RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:575047 CAPLUS
DN 137:140533
TI Preparation of 2,4,8-trisubstituted-8H-pyrido[2,3-d]pyrimidin-7-ones as CSBP/RK/p38 kinase inhibitors
IN Adams, Jerry L.; Boehm, Jeffrey C.; Hall, Ralph; Jin, Qi; Kasparec, Jiri; Silva, Domingos J.; Taggart, John J.
PA Smithkline Beecham Corporation, USA
SO PCT Int. Appl., 203 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002059083	A2	20020801	WO 2001-US50493	20011023
	WO 2002059083	A3	20030410		
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	NO 2003001794	A	20030623	NO 2003-1794	20030422
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	US 2001-310349P	P	20010806		
	US 2001-326618P	P	20011002		
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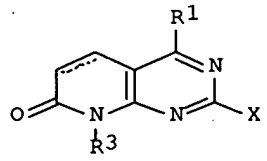
OS MARPAT 137:140533
GI



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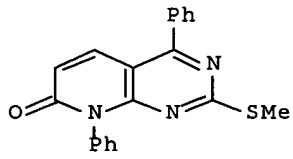


II

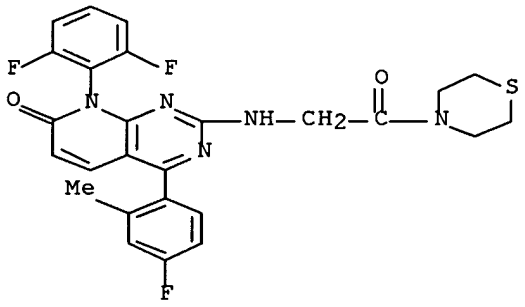
AB Title compds. I [wherein X = R2, OR2, SO0-2R2, (CH2)nNR10SO0-2R2, (CH2)nNR10COR2, (CH2)nNR4R14, or (CH2)nN(R2)2; R1 = (un)substituted (hetero)aryl; R2 = H, (un)substituted alkyl, cycloalkyl(alkyl), (hetero)aryl(alkyl), heterocyclyl(alkyl), alkylamino, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, etc.; R3 = (un)substituted alkyl, cycloalkyl(alkyl), (hetero)aryl(alkyl), or heterocyclyl; R4 and R14 = independently H or (un)substituted alkyl, cycloalkyl(alkyl), or aryl(alkyl); or NR4R14 = (un)substituted heterocyclyl; R10 = H or alkyl; n = 0-10] were prepd. as CSBP/p38 kinase inhibitors. For example, sequential coupling of 4,6-dichloro-2-methylsulfanylpyrimidine-5-carbaldehyde with aniline (76%) and phenylboronic acid (70%) gave 2-methylsulfanyl-4-phenyl-6-phenylaminopyrimidine-5-carbaldehyde.

Cyclization with bis(2,2,2-trifluoroethyl)(methoxycarbonylmethyl)phosphonate in the presence of 18-crown-6 and bis(trimethylsilyl)amide in THF afforded the 8H-pyrido[2,3-d]pyrimidin-7-one II (91%). The latter exhibited pos. inhibitory activity in the CSBP/p38 kinase binding assay with IC50 < 10 .mu.M. I are useful for the treatment of a variety of CSBP/p38 kinase mediated diseases, such as arthritis, sepsis, stroke, asthma, pulmonary disease, osteoporosis, congestive heart failure, the common cold or respiratory viral infections, etc. (no data).

IT **444608-52-0P**, 8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-(2-oxo-2-thiomorpholin-4-ylethylamino)-8H-pyrido[2,3-d]pyrimidin-7-one
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(CSBP/p38 kinase inhibitor; prepn. of pyridopyrimidinones as CSBP/RK/p38 kinase inhibitors by cyclization reactions of (phenylamino)pyrimidinecarbaldehyde derivs.)

RN 444608-52-0 CAPLUS

CN Thiomorpholine, 4-[[[8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-7,8-dihydro-7-oxopyrido[2,3-d]pyrimidin-2-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

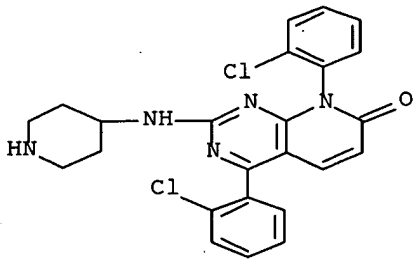


IT **444606-42-2P**, 4,8-Bis(2-chlorophenyl)-2-(piperidin-4-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one **444606-45-5P**, 4,8-Bis(2-chlorophenyl)-2-(1-methylpiperidin-4-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one **444606-67-1P**, 8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[(1-methylpiperidin-4-yl)amino]-8H-pyrido[2,3-d]pyrimidin-7-one **444607-45-8P**, 2-Cyclohexylamino-4-(4-fluoro-2-methylphenyl)-8-(2-fluorophenyl)-8H-pyrido[2,3-d]pyrimidin-7-one **444607-46-9P**, 2-(Tetrahydropyran-4-ylamino)-4-(4-fluoro-2-methylphenyl)-8-(2-fluorophenyl)-8H-pyrido[2,3-d]pyrimidin-7-one **444607-48-1P**, 2-Cyclohexylamino-4-(4-fluoro-2-methylphenyl)-8-(2,6-difluorophenyl)-8H-pyrido[2,3-d]pyrimidin-7-one **444607-49-2P**, 2-(Tetrahydropyran-4-ylamino)-4-(4-fluoro-2-methylphenyl)-8-(2,6-difluorophenyl)-8H-pyrido[2,3-d]pyrimidin-7-one **444607-51-6P**, trans-2-(4-Hydroxycyclohexylamino)-4-(4-fluoro-2-methylphenyl)-8-(2-fluorophenyl)-8H-pyrido[2,3-d]pyrimidin-7-one **444607-54-9P**, trans-2-(4-Hydroxycyclohexylamino)-4-(4-fluoro-2-methylphenyl)-8-(2,6-difluorophenyl)-8H-pyrido[2,3-d]pyrimidin-7-one **444607-58-3P**, 1-[2-[[8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-2-yl]amino]ethyl]-3-phenylurea

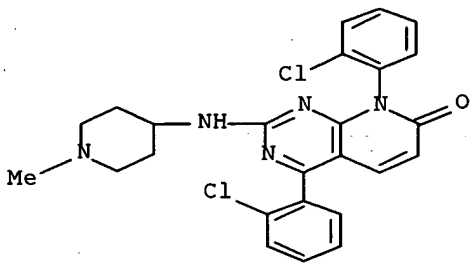
444607-59-4P, 1-[2-[[8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-2-yl]amino]ethyl]-3-cyclohexylurea **444607-60-7P**, 1-[2-[[8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-2-yl]amino]ethyl]-3-(3-fluorophenyl)urea **444607-62-9P** **444607-67-4P** **444607-74-3P** **444607-95-8P** **444607-97-0P**, 4-(4-Fluoro-2-methylphenyl)-2-[(trans-4-hydroxycyclohexyl)amino]-8-o-tolyl-8H-pyrido[2,3-d]pyrimidin-7-one **444608-03-1P**, 2-Cyclohexylamino-4-(4-fluoro-2-methylphenyl)-8-o-tolyl-8H-pyrido[2,3-d]pyrimidin-7-one **444608-05-3P**, 4-(4-Fluoro-2-methylphenyl)-2-(tetrahydropyran-4-ylamino)-8-o-tolyl-8H-pyrido[2,3-d]pyrimidin-7-one **444608-13-3P**, 8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[(2-oxo-2-pyrrolidin-1-ylethyl)amino]-8H-pyrido[2,3-d]pyrimidin-7-one **444608-16-6P**, 4-(4-Fluoro-2-methylphenyl)-2-morpholin-4-yl-8-o-tolyl-8H-pyrido[2,3-d]pyrimidin-7-one **444608-18-8P**, 8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[[(1SR,2SR)-2-hydroxycyclohexyl]amino]-8H-pyrido[2,3-d]pyrimidin-7-one **444608-22-4P**, 8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[[2-(1H-tetrazol-5-yl)ethyl]amino]-8H-pyrido[2,3-d]pyrimidin-7-one **444608-23-5P**, N-Cyclopropyl-2-[[8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-2-yl]amino]acetamide **444608-25-7P**, 8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[(1H-tetrazol-5-ylmethyl)amino]-8H-pyrido[2,3-d]pyrimidin-7-one **444608-28-0P**, 8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[(1SR,2SR)-2-hydroxycyclopentylamino]-8H-pyrido[2,3-d]pyrimidin-7-one **444608-31-5P**, 8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[[2-oxo-2-(3-oxopiperazin-1-yl)ethyl]amino]-8H-pyrido[2,3-d]pyrimidin-7-one **444608-32-6P**, 8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[[(5-methyl-4H-[1,2,4]triazol-3-yl)methyl]amino]-8H-pyrido[2,3-d]pyrimidin-7-one **444608-33-7P**, 8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[(1,1-dioxotetrahydro-1-thiophen-3-ylmethyl)amino]-8H-pyrido[2,3-d]pyrimidin-7-one **444608-35-9P**, 8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[(3-methylisoxazol-5-ylmethyl)amino]-8H-pyrido[2,3-d]pyrimidin-7-one **444608-37-1P**, 8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[[(3S,4S)-4-hydroxy-1,1-dioxotetrahydrothiophen-3-yl]amino]-8H-pyrido[2,3-d]pyrimidin-7-one **444608-39-3P**, 8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[(2-oxo-2,3-dihydropyrimidin-4-yl)amino]-8H-pyrido[2,3-d]pyrimidin-7-one **444608-40-6P**, 8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[(1H-imidazol-2-ylmethyl)amino]-8H-pyrido[2,3-d]pyrimidin-7-one **444608-41-7P**, 8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[(1H-[1,2,4]triazol-3-yl)amino]-8H-pyrido[2,3-d]pyrimidin-7-one **444608-42-8P**, 8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-(1H-tetrazol-5-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one **444608-44-0P**, 8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-(tetrahydrofuran-3-ylamino)-8H-pyrido[2,3-d]pyrimidin-7-one **444608-47-3P**, 8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[[2-(1H-imidazol-4-yl)ethyl]amino]-8H-pyrido[2,3-d]pyrimidin-7-one **444608-49-5P**, Cyclopropanecarboxylic acid [8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidine-2-yl]amide **444608-51-9P**, Cyclopropanecarboxylic acid (1-

cyclopropylmethanoyl)[8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-2-yl]amide **444608-53-1P**, 8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[(tetrahydrofuran-2-ylmethyl)amino]-8H-pyrido[2,3-d]pyrimidin-7-one **444608-54-2P**, 8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[[2-(3-hydroxyazetidin-1-yl)-2-oxoethyl]amino]-8H-pyrido[2,3-d]pyrimidin-7-one **444608-57-5P**, (1SR,2RS)-2-[[8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-7-oxo-7,8-dihydropyrido[2,3-d]pyrimidin-2-yl]amino]cyclopentanecarboxamide **444608-61-1P**, 8-(2,6-Difluorophenyl)-2-[[2-(1,1-dioxothiomorpholin-4-yl)-2-oxoethyl]amino]-4-(4-fluoro-2-methylphenyl)-8H-pyrido[2,3-d]pyrimidin-7-one **444608-62-2P**, 8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[3-(2-oxopyrrolidin-1-yl)propylamino]-8H-pyrido[2,3-d]pyrimidin-7-one **444608-65-5P**, 8-(2,6-Difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[[2-(5-oxo-4,5-dihydro[1,2,4]oxadiazol-3-yl)ethyl]amino]-8H-pyrido[2,3-d]pyrimidin-7-one
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CSBP/p38 kinase inhibitor; prepn. of pyridopyrimidinones as CSBP/RK/p38 kinase inhibitors by cyclization reactions of (phenylamino)pyrimidinecarbaldehyde derivs.)

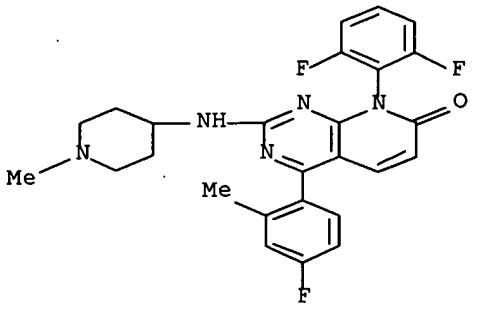
RN 444606-42-2 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 4,8-bis(2-chlorophenyl)-2-(4-piperidinylamino)- (9CI) (CA INDEX NAME)



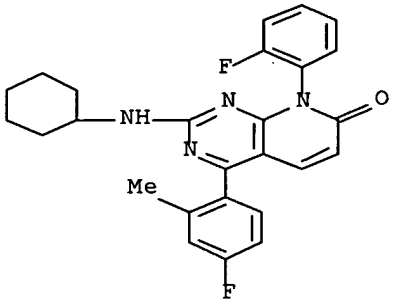
RN 444606-45-5 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 4,8-bis(2-chlorophenyl)-2-[(1-methyl-4-piperidinyl)amino]- (9CI) (CA INDEX NAME)



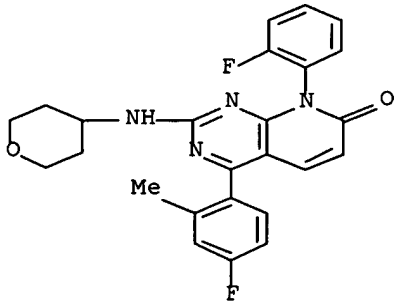
RN 444606-67-1 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[(1-methyl-4-piperidinyl)amino]- (9CI) (CA INDEX NAME)



RN 444607-45-8 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 2-(cyclohexylamino)-4-(4-fluoro-2-methylphenyl)-8-(2-fluorophenyl)- (9CI) (CA INDEX NAME)

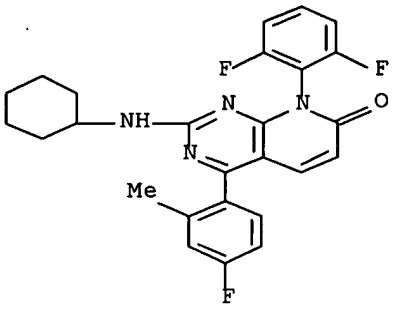


RN 444607-46-9 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 4-(4-fluoro-2-methylphenyl)-8-(2-fluorophenyl)-2-[(tetrahydro-2H-pyran-4-yl)amino]- (9CI) (CA INDEX NAME)

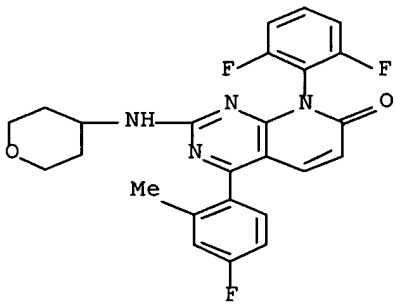


RN 444607-48-1 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 2-(cyclohexylamino)-8-(2,6-

difluorophenyl)-4-(4-fluoro-2-methylphenyl)- (9CI) (CA INDEX NAME)

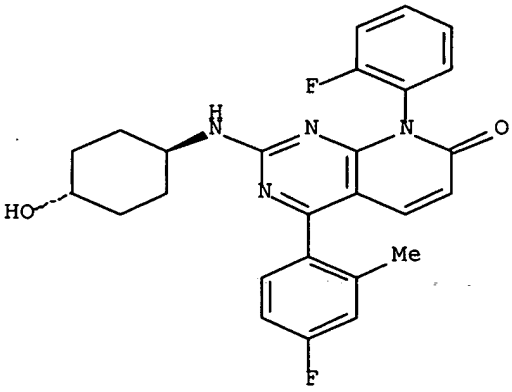


RN 444607-49-2 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[(tetrahydro-2H-pyran-4-yl)amino]- (9CI) (CA INDEX NAME)



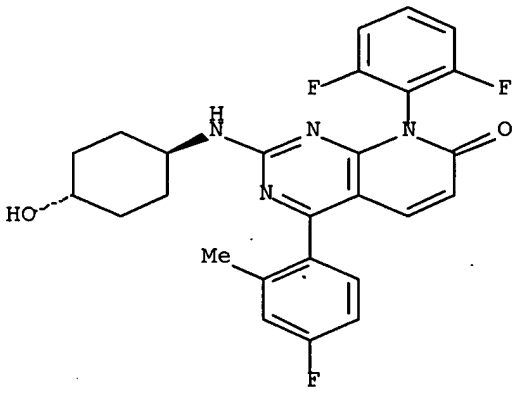
RN 444607-51-6 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 4-(4-fluoro-2-methylphenyl)-8-(2-fluorophenyl)-2-[(trans-4-hydroxycyclohexyl)amino]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

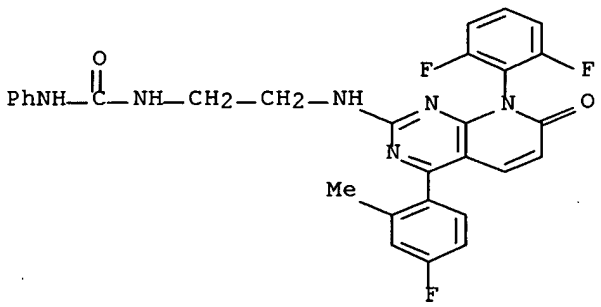


RN 444607-54-9 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[(trans-4-hydroxycyclohexyl)amino]- (9CI) (CA INDEX NAME)

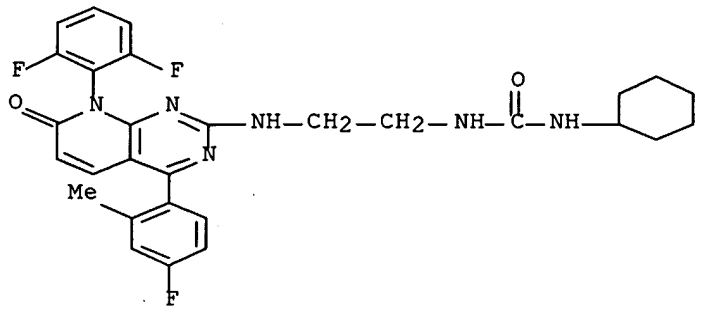
Relative stereochemistry.



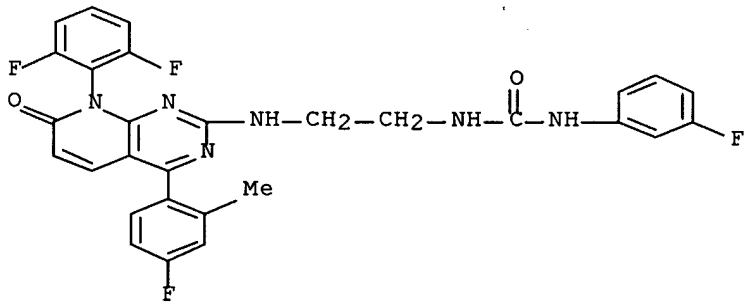
RN 444607-58-3 CAPLUS
CN Urea, N-[2-[[8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-7,8-dihydro-7-oxopyrido[2,3-d]pyrimidin-2-yl]amino]ethyl]-N'-phenyl- (9CI) (CA INDEX NAME)



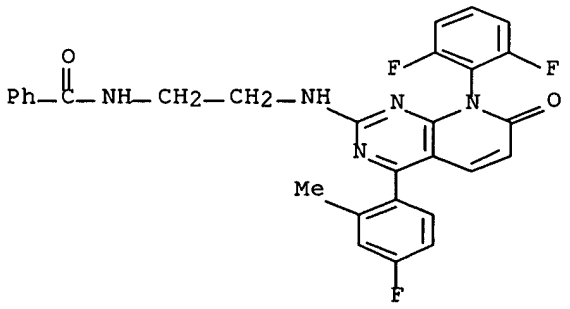
RN 444607-59-4 CAPLUS
CN Urea, N-cyclohexyl-N'-[2-[[8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-7,8-dihydro-7-oxopyrido[2,3-d]pyrimidin-2-yl]amino]ethyl]- (9CI) (CA INDEX NAME)



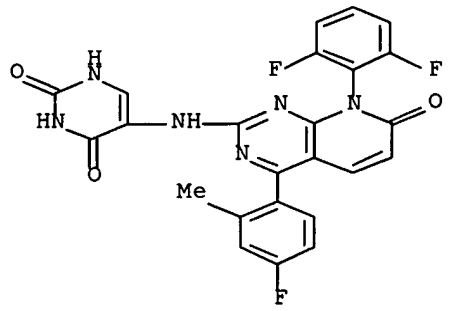
RN 444607-60-7 CAPLUS
CN Urea, N-[2-[[8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-7,8-dihydro-7-oxopyrido[2,3-d]pyrimidin-2-yl]amino]ethyl]-N'-(3-fluorophenyl)-
(9CI) (CA INDEX NAME)



RN 444607-62-9 CAPLUS
CN Benzamide, N-[2-[[8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-7,8-
dihydro-7-oxopyrido[2,3-d]pyrimidin-2-yl]amino]ethyl]- (9CI) (CA INDEX NAME)

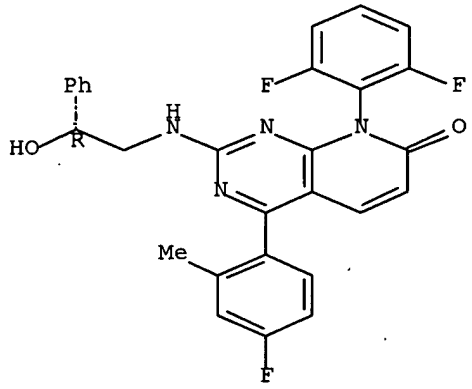


RN 444607-67-4 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-[[8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-7,8-dihydro-7-oxopyrido[2,3-d]pyrimidin-2-yl]amino]- (9CI) (CA INDEX NAME)

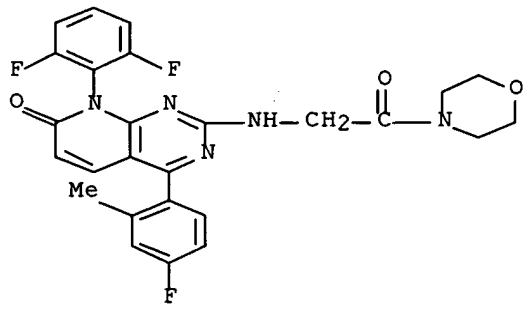


RN 444607-74-3 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[[(2R)-2-hydroxy-2-phenylethyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



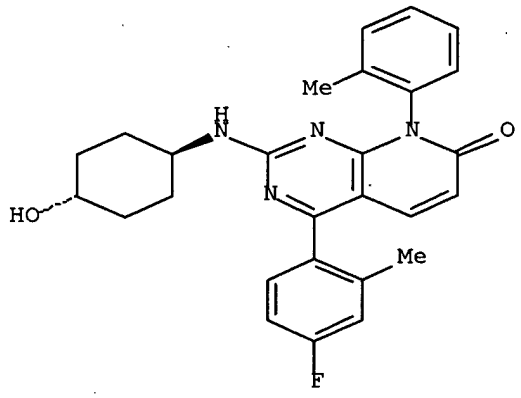
RN 444607-95-8 CAPLUS
CN Morpholine, 4-[[[8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-7,8-dihydro-7-oxopyrido[2,3-d]pyrimidin-2-yl]amino]acetyl]- (9CI) (CA INDEX NAME)



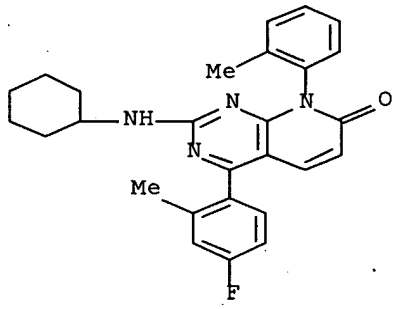
RN 444607-97-0 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 4-(4-fluoro-2-methylphenyl)-2-[(trans-

4-
hydroxycyclohexyl)amino]-8-(2-methylphenyl)- (9CI) (CA INDEX NAME)

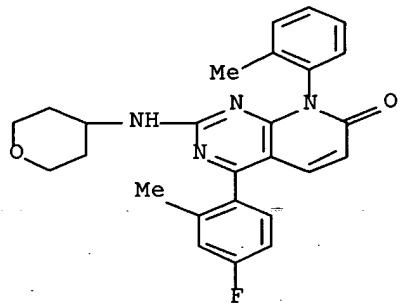
Relative stereochemistry.



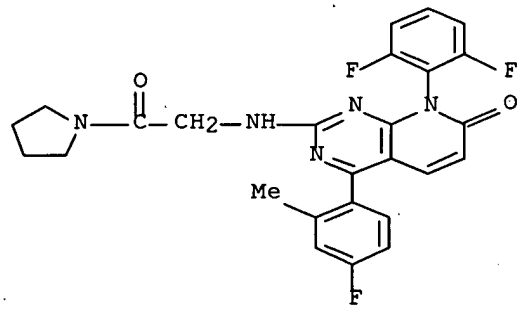
RN 444608-03-1 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 2-(cyclohexylamino)-4-(4-fluoro-2-methylphenyl)-8-(2-methylphenyl)- (9CI) (CA INDEX NAME)



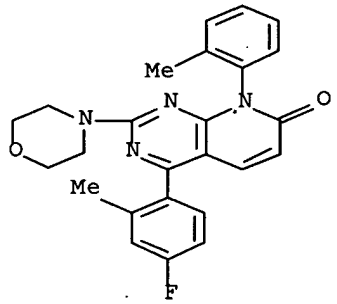
RN 444608-05-3 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 4-(4-fluoro-2-methylphenyl)-8-(2-methylphenyl)-2-[(tetrahydro-2H-pyran-4-yl)amino]- (9CI) (CA INDEX NAME)



RN 444608-13-3 CAPLUS
CN Pyrrolidine, 1-[[[8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-7,8-
dihydro-7-oxopyrido[2,3-d]pyrimidin-2-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

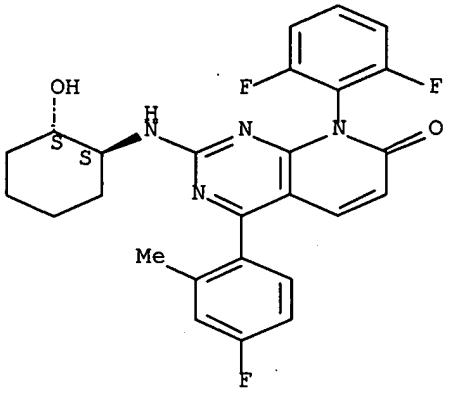


RN 444608-16-6 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 4-(4-fluoro-2-methylphenyl)-8-(2-methylphenyl)-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)

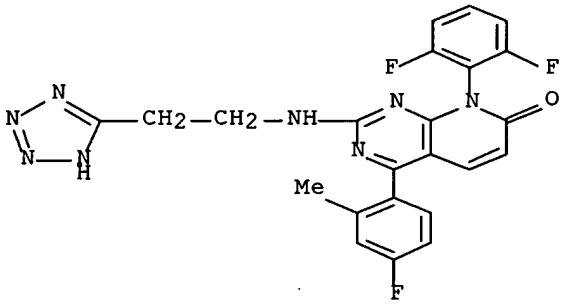


RN 444608-18-8 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[[(1R,2R)-2-hydroxycyclohexyl]amino]-, rel- (9CI) (CA INDEX NAME)

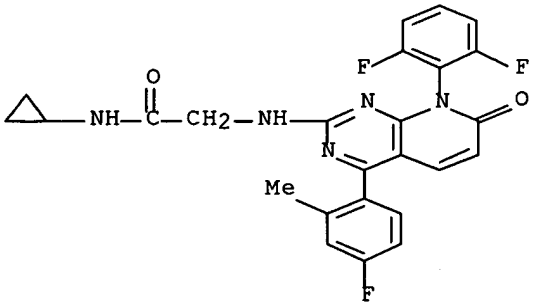
Relative stereochemistry.



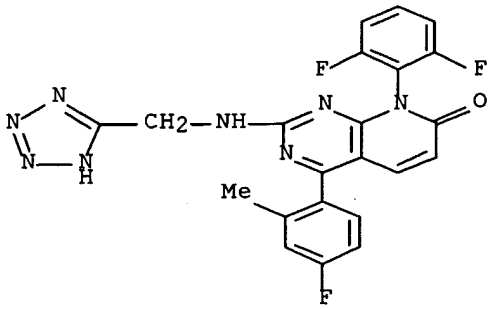
RN 444608-22-4 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[[2-(1H-tetrazol-5-yl)ethyl]amino]- (9CI) (CA INDEX NAME)



RN 444608-23-5 CAPLUS
CN Acetamide, N-cyclopropyl-2-[[8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-7,8-dihydro-7-oxopyrido[2,3-d]pyrimidin-2-yl]amino]- (9CI) (CA INDEX NAME)

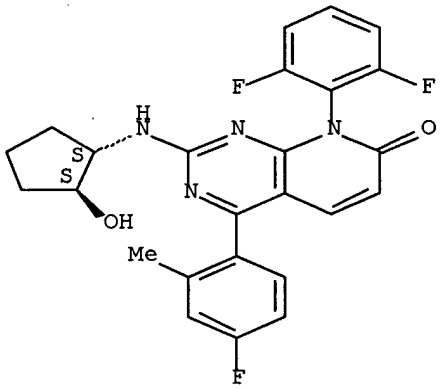


RN 444608-25-7 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[(1H-tetrazol-5-ylmethyl)amino]- (9CI) (CA INDEX NAME)

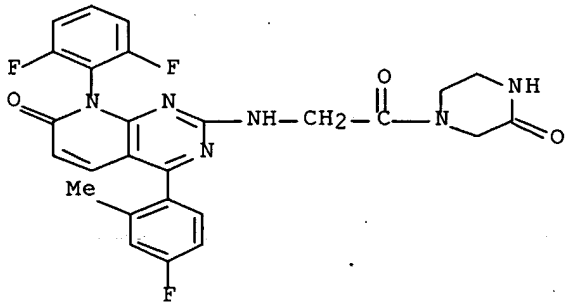


RN 444608-28-0 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[[(1R,2R)-2-hydroxycyclopentyl]amino]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

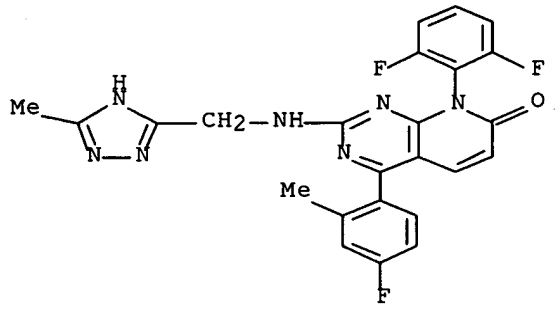


RN 444608-31-5 CAPLUS
CN Piperazinone, 4-[[[8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-7,8-dihydro-7-oxopyrido[2,3-d]pyrimidin-2-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

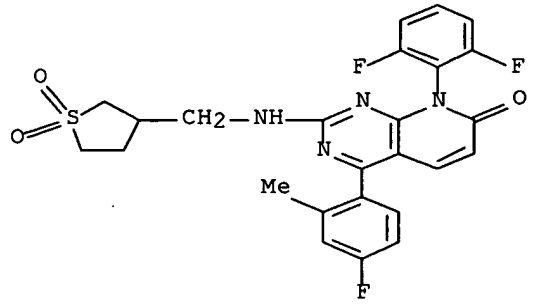


RN 444608-32-6 CAPLUS

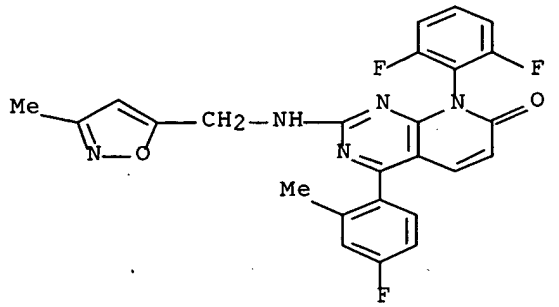
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[[(5-methyl-1H-1,2,4-triazol-3-yl)methyl]amino]- (9CI) (CA INDEX NAME)



RN 444608-33-7 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[[(tetrahydro-1,1-dioxido-3-thienyl)methyl]amino]- (9CI) (CA INDEX NAME)



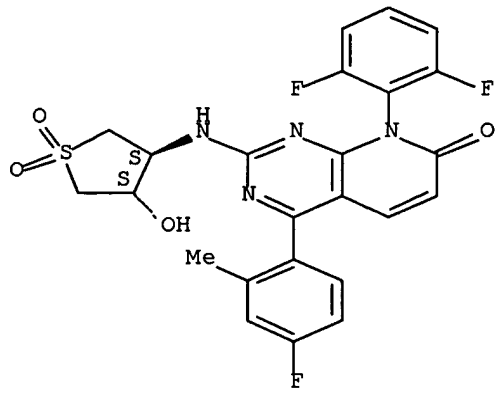
RN 444608-35-9 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[[(3-methyl-5-isoxazolyl)methyl]amino]- (9CI) (CA INDEX NAME)



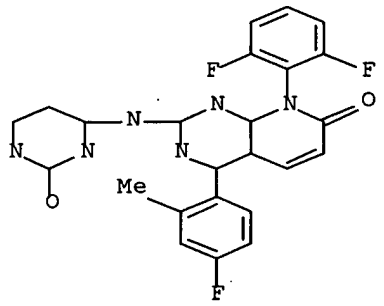
RN 444608-37-1 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-(2,6-difluorophenyl)-4-(4-fluoro-2-

methylphenyl)-2-[[(3S,4S)-tetrahydro-4-hydroxy-1,1-dioxido-3-thienyl]amino]- (9CI) (CA INDEX NAME)

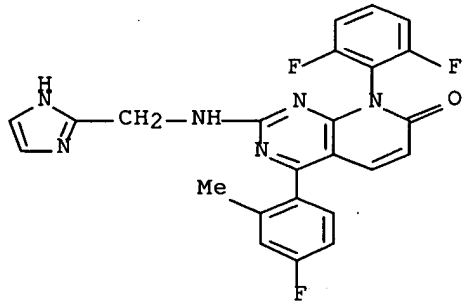
Absolute stereochemistry.



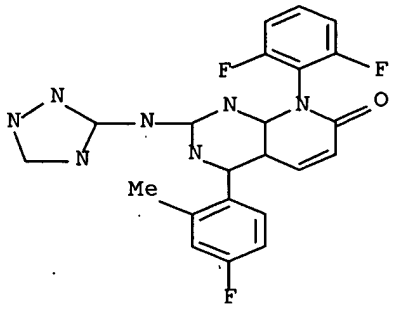
RN 444608-39-3 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-(2,6-difluorophenyl)-2-[(1,2-dihydro-2-oxo-4-pyrimidinyl)amino]-4-(4-fluoro-2-methylphenyl)- (9CI) (CA INDEX NAME)



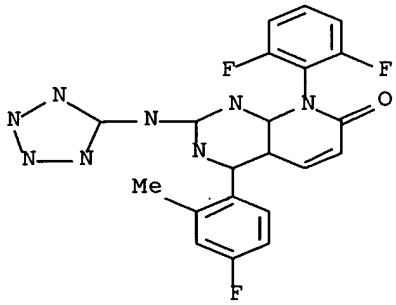
*** FRAGMENT DIAGRAM IS INCOMPLETE
RN 444608-40-6 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[(1H-imidazol-2-ylmethyl)amino]- (9CI) (CA INDEX NAME)



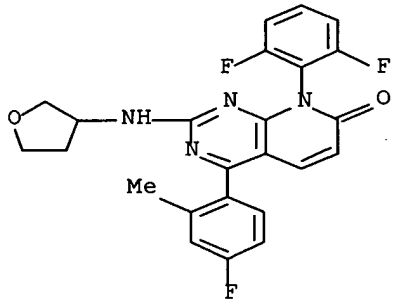
RN 444608-41-7 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-(1H-1,2,4-triazol-3-ylamino)- (9CI) (CA INDEX NAME)



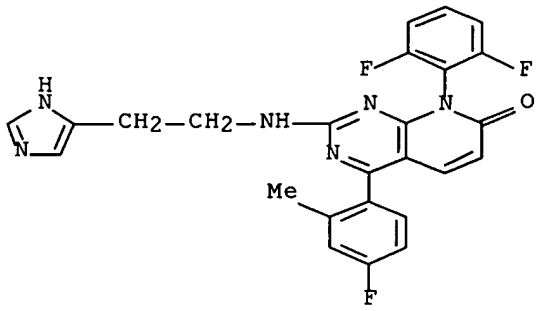
*** FRAGMENT DIAGRAM IS INCOMPLETE
RN 444608-42-8 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-(1H-tetrazol-5-ylamino)- (9CI) (CA INDEX NAME)



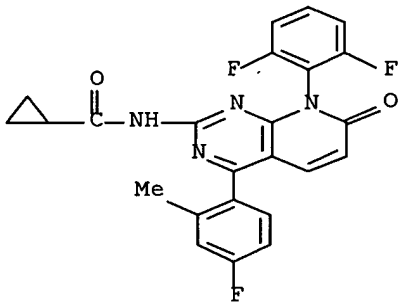
*** FRAGMENT DIAGRAM IS INCOMPLETE
RN 444608-44-0 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[(tetrahydro-3-furanyl)amino]- (9CI) (CA INDEX NAME)



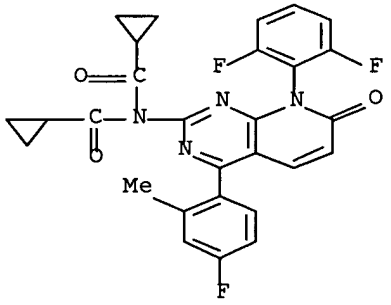
RN 444608-47-3 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[[2-(1H-imidazol-4-yl)ethyl]amino]- (9CI) (CA INDEX NAME)



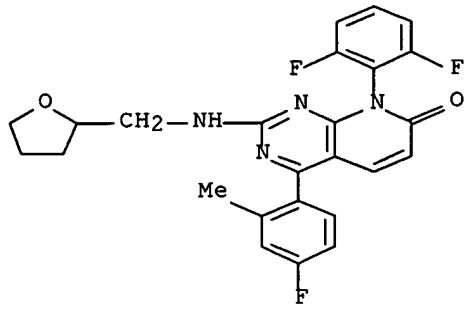
RN 444608-49-5 CAPLUS
CN Cyclopropanecarboxamide, N-[8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-7,8-dihydro-7-oxopyrido[2,3-d]pyrimidin-2-yl]- (9CI) (CA INDEX NAME)



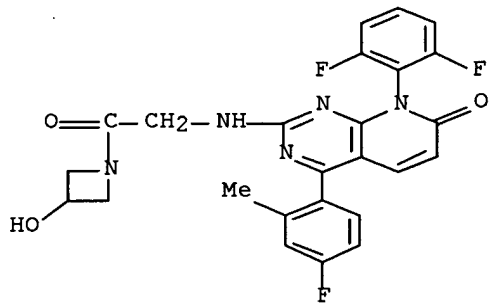
RN 444608-51-9 CAPLUS
CN Cyclopropanecarboxamide, N-(cyclopropylcarbonyl)-N-[8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-7,8-dihydro-7-oxopyrido[2,3-d]pyrimidin-2-yl]-(9CI) (CA INDEX NAME)



RN 444608-53-1 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[[(tetrahydro-2-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)

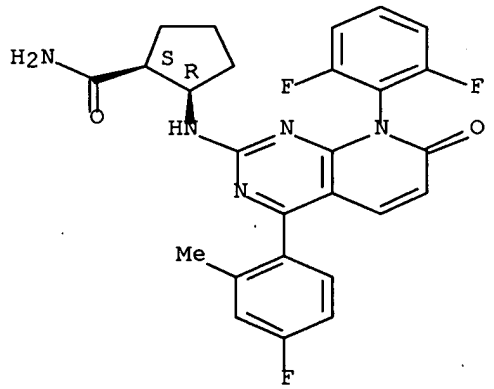


RN 444608-54-2 CAPLUS
CN 3-Azetidinol, 1-[[[8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-7,8-dihydro-7-oxopyrido[2,3-d]pyrimidin-2-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

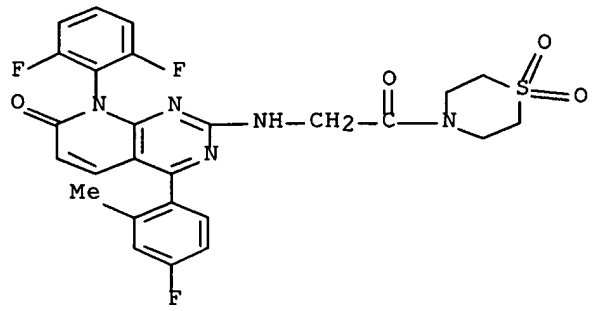


RN 444608-57-5 CAPLUS
CN Cyclopentanecarboxamide, 2-[[8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-7,8-dihydro-7-oxopyrido[2,3-d]pyrimidin-2-yl]amino]-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

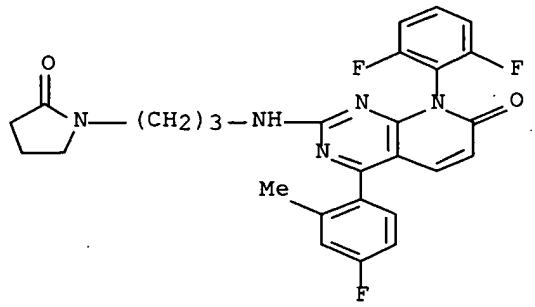
Relative stereochemistry.



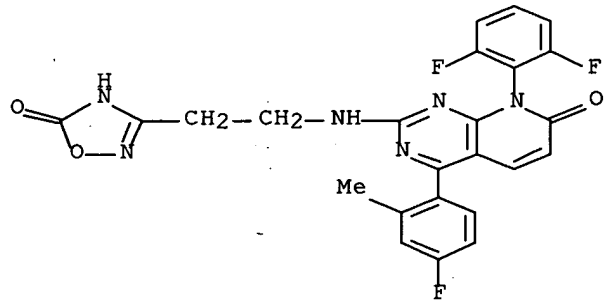
RN 444608-61-1 CAPLUS
CN Thiomorpholine, 4-[[[8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-7,8-dihydro-7-oxopyrido[2,3-d]pyrimidin-2-yl]amino]acetyl]-, 1,1-dioxide (9CI) (CA INDEX NAME)



RN 444608-62-2 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-(2,6-difluorophenyl)-4-(4-fluoro-2-methylphenyl)-2-[[3-(2-oxo-1-pyrrolidinyl)propyl]amino]- (9CI) (CA INDEX NAME)



RN 444608-65-5 CAPLUS
CN Pyrido[2,3-d]pyrimidin-7(8H)-one, 8-(2,6-difluorophenyl)-2-[[2-(2,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl)ethyl]amino]-4-(4-fluoro-2-methylphenyl)- (9CI) (CA INDEX NAME)



L7 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2002:357940 CAPLUS

DN 137:78846

TI An Expedient Synthesis of Highly Functionalized Naphthyridones and Quinolines from a Common N-Aryl Pyridinone Template

AU Savarin, Cecile G.; Murry, Jerry A.; Dormer, Peter G.

CS Department of Process Research, Merck Research Laboratories, Rahway, NJ, 07065, USA

SO Organic Letters (2002), 4(12), 2071-2074
CODEN: ORLEF7; ISSN: 1523-7060

PB American Chemical Society

DT Journal

LA English

OS CASREACT 137:78846

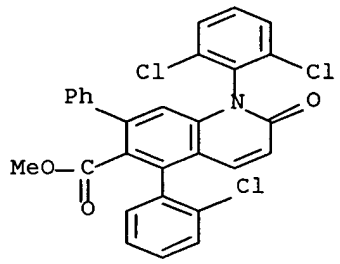
AB The authors describe a new base-mediated process for the formation of N-arylpyridinones and their use for the prepn. of naphthyridones and quinolines. The cyclization of various hindered enamines with Me propiolate proceeds efficiently in the presence of NaOH to afford the corresponding N-arylpyridinones. These substrates were then found to undergo subsequent cyclizations to afford highly functionalized naphthyridones and quinolines.

IT **439942-70-8P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of naphthyridones and quinolines from N-arylpyridinones)

RN 439942-70-8 CAPLUS

CN 6-Quinolinecarboxylic acid, 5-(2-chlorophenyl)-1-(2,6-dichlorophenyl)-1,2-dihydro-2-oxo-7-phenyl-, methyl ester (9CI) (CA INDEX NAME)

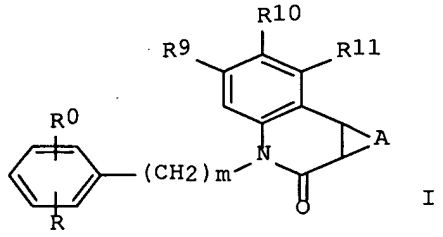


RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:283958 CAPLUS
DN 134:311201
TI Preparation of isoxazoloquinolinones as inhibitors of multidrug resistance protein 1.
IN Bonjouklian, Rosanne; Johnson, Douglas Webb; Lander, Peter Ambrose; Lohman, Mark Christopher; Patel, Vinod Francis; Vepachedu, Sreenivasarao; Xie, Yongping
PA Eli Lilly and Company, USA
SO PCT Int. Appl., 160 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001027116	A2	20010419	WO 2000-US21980	20000922
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1224189	A2	20020724	EP 2000-968314	20000922
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
PRAI	US 1999-158175P	P	19991007		
	US 1999-169784P	P	19991209		
	WO 2000-US21980	W	20000922		

OS MARPAT 134:311201
GI



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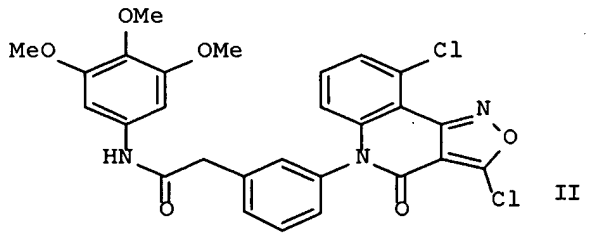


II

AB Title compds. [I; A = atoms to form a 5-membered (substituted) heteroaryl ring contg. N and a 2nd heteroatom selected from N, O, S; R = (CH2)mCHR1NHR2, OCH2CH2NHR2, NHR2, etc.; R0 = H, OH, alkyl, phenylalkyl, cycloalkylalkyl; m = 0-2; R1 = H, alkyl; R2 = H, COR6, SO2R7, etc.; R6 = alkyl, substituted cycloalkyl, aryl, OCMe3, heterocyclyl,

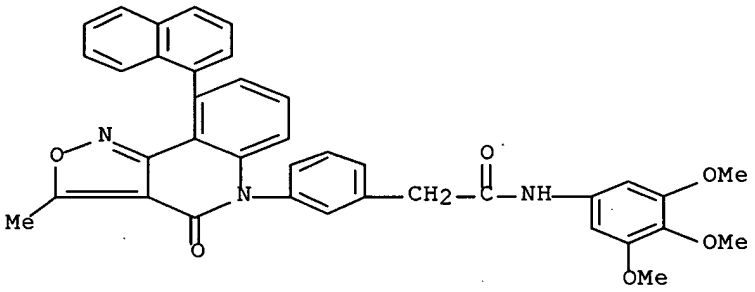
heterocyclylalkyl, etc.; R7 = alkyl, (substituted) Ph; R9-R11 = H, halo, CO2R1, (substituted) aryl, thienyl, alkoxy, alkylphenyl, alkenyl], were prepd. Thus, N-(3,4,5-trimethoxyphenyl)-3-[3-(2-chloro-5-fluorophenyl)-5-chloroisoxazol-4-oyl]aminophenylacetamide (prepn. given) was stirred with K2CO3 at -10.degree. for 3 h to give 31.1% title compd. (II). I were said to demonstrate a significant effect in reversing MRP1 multiple drug resistance. I drug formulations are given.

IT **334970-84-2P 334970-85-3P 334970-86-4P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)(prepn. of isoxazoloquinolinones as inhibitors of multidrug resistance protein 1)

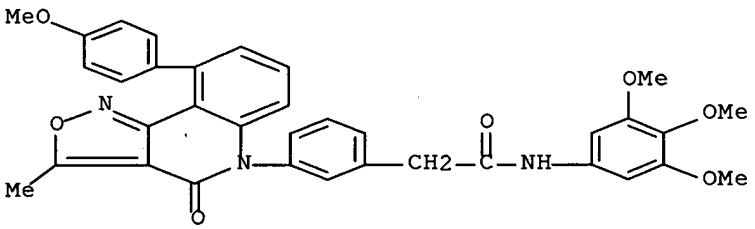
RN 334970-84-2 CAPLUS

CN Benzeneacetamide, 3-[3-methyl-9-(1-naphthalenyl)-4-oxoisoxazolo[4,3-c]quinolin-5(4H)-yl]-N-(3,4,5-trimethoxyphenyl)- (9CI) (CA INDEX NAME)



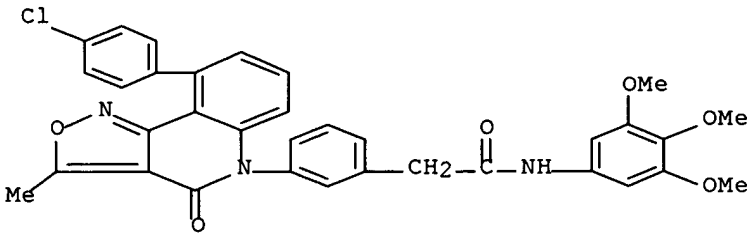
RN 334970-85-3 CAPLUS

CN Benzeneacetamide, 3-[9-(4-methoxyphenyl)-3-methyl-4-oxoisoxazolo[4,3-c]quinolin-5(4H)-yl]-N-(3,4,5-trimethoxyphenyl)- (9CI) (CA INDEX NAME)

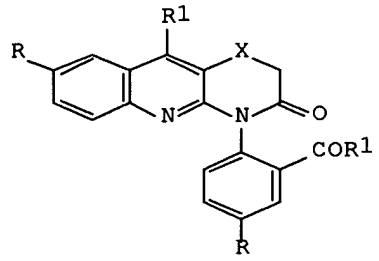


RN 334970-86-4 CAPLUS

CN Benzeneacetamide, 3-[9-(4-chlorophenyl)-3-methyl-4-oxoisoxazolo[4,3-c]quinolin-5(4H)-yl]-N-(3,4,5-trimethoxyphenyl)- (9CI) (CA INDEX NAME)



L7 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1977:584455 CAPLUS
DN 87:184455
TI Heterocycles from 2-amino ketones. XXIII. Reaction of o-amino ketones with dicarboxylic acids
AU Kempter, G.; Rehbaum, D.; Schirmer, J.
CS Sekt. Chem./Biol., Paedagog. Hochsch. "Karl Liebknecht", Potsdam, Ger. Dem. Rep.
SO Journal fuer Praktische Chemie (Leipzig) (1977), 319(4), 589-600
CODEN: JPCEAO; ISSN: 0021-8383
DT Journal
LA German
GI



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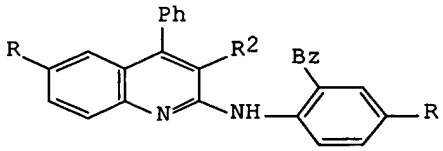
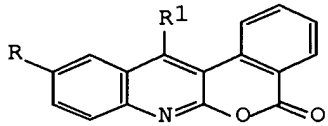
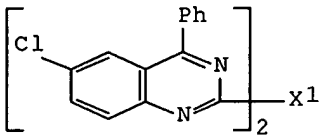


II

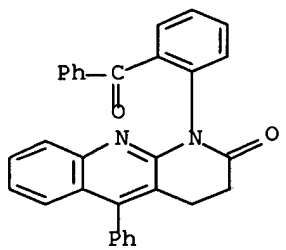


III

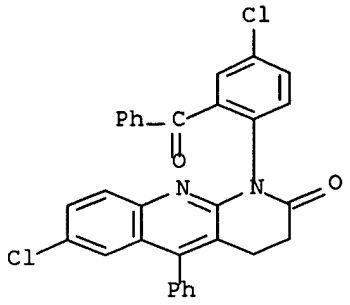


IV

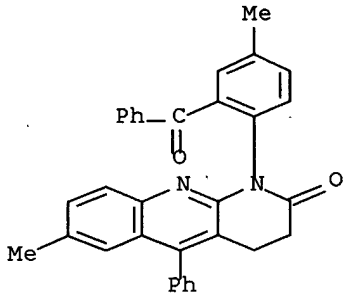
AB Condensed quinolines I (X = CH2, S, O; R = H, Cl, Me; R1 = Ph, 4-MeC6H4) were obtained by condensing aminobenzophenones 4,2-R(R1CO)C6H3NH2 with (HO2CCH2)2X. Reaction of HO2C(CH2)n+1CO2H (n = 3, 4, 7) or o-HO2CC6H4CH2CH2CO2H with 4,2-RBzC6H3NH2 (R = H, Cl, Br, NO2) gave II [R2 = (CH2)nCO2H, o-CH2C6H4OC2H]. III were similarly obtained with homophthalic acid. Reaction of acid chlorides ClCOX1COCl [X1 = (CH2)m, CH2SCH2, CH2OCH2; m = 3, 4, 8] with 4,2-ClBzC6H3NH2 gave (4,2-ClBzC6H3NHCO)2X1 which cyclized to IV with NH3.
IT **64571-72-8P 64571-73-9P 64571-74-0P 64571-75-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)(prepn. of)
RN 64571-72-8 CAPLUS
CN Benzo[b][1,8]naphthyridin-2(1H)-one, 1-(2-benzoylphenyl)-3,4-dihydro-5-phenyl- (9CI) (CA INDEX NAME)



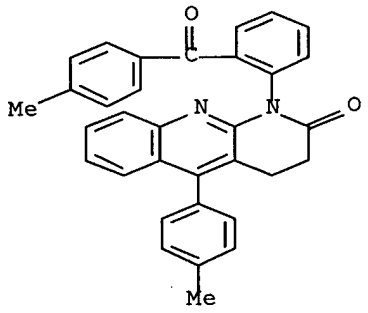
RN 64571-73-9 CAPLUS
CN Benzo[b][1,8]naphthyridin-2(1H)-one, 1-(2-benzoyl-4-chlorophenyl)-7-chloro-3,4-dihydro-5-phenyl- (9CI) (CA INDEX NAME)



RN 64571-74-0 CAPLUS
CN Benzo[b][1,8]naphthyridin-2(1H)-one, 1-(2-benzoyl-4-methylphenyl)-3,4-dihydro-7-methyl-5-phenyl- (9CI) (CA INDEX NAME)



RN 64571-75-1 CAPLUS
CN Benzo[b][1,8]naphthyridin-2(1H)-one, 3,4-dihydro-1-[2-(4-methylbenzoyl)phenyl]-5-(4-methylphenyl)- (9CI) (CA INDEX NAME)



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=> d l1; d l3; d his; log y
L1 HAS NO ANSWERS
L1                STR
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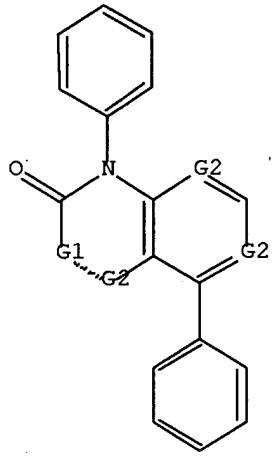
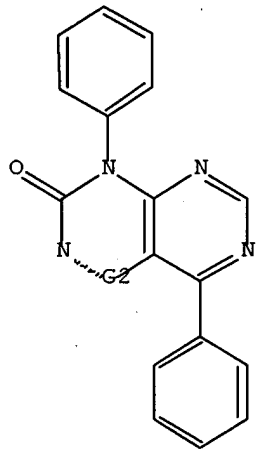


Cy

G1 C,O,N
G2 C,N

Structure attributes must be viewed using STN Express query preparation.

L3 HAS NO ANSWERS
L3 STR



Cy

G1 C,O,N
G2 C,N

Structure attributes must be viewed using STN Express query preparation.

(FILE 'HOME' ENTERED AT 16:20:53 ON 29 OCT 2003)

FILE 'REGISTRY' ENTERED AT 16:21:00 ON 29 OCT 2003

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L1                STRUCTURE UPLOADED
L2            588 S L1 FUL
L3                STRUCTURE UPLOADED
L4              5 S L3 SAM SUB=L2
L5             80 S L3 FUL SUB=L2
L6            508 S L2 NOT L5
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FILE 'CAPLUS' ENTERED AT 16:22:58 ON 29 OCT 2003

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L7              9 S L6
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	42.49	226.55

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-5.86	-5.86

STN INTERNATIONAL LOGOFF AT 16:25:13 ON 29 OCT 2003